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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/531,966	04/20/2005	Carl T Wittwer	P00950-US-01	8958

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07/26/2007

EXAMINER

CHUNDURU, SURYAPRABHA

ART UNIT	PAPER NUMBER
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1637

MAIL DATE	DELIVERY MODE
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PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/531,966	Applicant(s) WITTWER ET AL.	
	Examiner Suryaprabha Chunduru	Art Unit 1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 10 July 2007.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 2,3,17-20,23-30,33-35,37,39-43,45-51,53,55-58,61,65 and 66 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 2,3,17-20,23-30,33-35,37,39-43,45-51,53,55-58,61,65 and 66 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 20 April 2005 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>4/20/05</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

1. Applicant's election of Group I (claims 2-3, 17-20, 23-30, 33-35, 37, 39-43, 45-51, 53, 55-58, 61, 65-66) in the reply filed on July 10, 2007 is acknowledged. Applicants amended claims 49-51, 53, 55-58, and 61 along with the response to the restriction requirement. Applicants' arguments regarding the Ririe et al. reference are fully considered and found persuasive. However, Examiner herewith provides a reference that anticipates the independent claim 24. hence the lack of unity still deemed proper.

Status of Application

2. Claims 2-3, 17-20, 23-30, 33-35, 37, 39-43, 45-51, 53, 55-58, 61, 65-66 are considered for examination in this office action. Claims 1, 4-16, 21-2231-32, 36, 38, 44, 52, 54, 59-60, 62-64 are cancelled.

Priority

3. This application filed on April 20, 2005 is a 371 of PCT/US03/33429 filed on 10/22/2003, which claims benefit of US provisional 60/420,717 filed on 10/23/2002 and 60/439,978 filed on 01/14/2003.

Information Disclosure Statement

4. The Information Disclosure Statement filed on April 20, 2005 has been considered.

Claim Rejections - 35 USC § 102

5. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 2-3, 17-20, 23-28, 30, 33-35, 37, 39-43, 45-48 are rejected under 35

U.S.C. 102(b) as being anticipated by Wittwer et al. (USPN. 6,174,670).

Wittwer et al. teach a PCR reaction mixture comprising a target nucleic acid, PCR reagents, oligonucleotide primers configured for amplifying the target nucleic acid and a dsDNA binding dye having a percent saturation of at least 50% (see col. 30, line 61-67, col. 31, line 1-4, Fig. 15); Wittwer et al. also teach that (i) the dye has excitation between 410-500nm (see col. 22, line 54-60); (ii) genotyping using different dilutions of the dye and melting temperature analysis and comparing the meting curves (see col. 18, line 20-67, col. 15, line 8-19, col. 37, line 49-67, col. 18, line 20-22); (iii) dye is selected from SYBR green I and YO-PRO-1 (see col. 11, line 10-38, col. 22, line 1-26).

With regard to claim 2-3, Wittwer et al. teach that the binding dye saturation is of at least 80% or at least 100% (see Fig.15, col. 17, line 1-5).

With regard to claim 17, 20, Wittwer et al. teach generating melting curves from amplified product and identifying genotypes, single nucleotide polymorphisms and identifying hetero and homoduplexes (see col. 9, line 16-67, col. 10, line 1-36, col. 68, line 10-53, col. 14, line 30-67, col. 15, line 1-19).

With regard to claim 18-19, Wittwer et al. teach that the monitoring step is performed using fluorimeter having an excitation range of 450-490nm and an emission detection range of 510-530nm and the dye has an excitation maximum in a range of 410-465nm and an emission maximum is in the range of 450-500nm (see col. 22, line 54-66).

With regard to claim 23, Wittwer et al. teach that the method comprises mutation scanning on first and second samples and comparing the melting curves (see col. 14, line 30-67, col. 15, line 1-19, col.69, line 11-55).

With regard to claim 25-28, 37, Wittwer et al. teach that the method comprises normalizing magnitude of melting curve and repeating the normalizing steps with at least one additional target nucleic acid comparing the normalized curves and plotting the fluorescence difference between normalized curves, and plotting temperature shifted curves (see col. 71, line 15-67, col. 17, line 1-46, Fig. 13-26).

With regard to claim 30, Wittwer et al teach the dyes include SYGR Green, YO-PRO-1, acridine orange (see col. 11,line 26-38, col. 71, line 8-12).

With regard to claim 33-34, Wittwer et al. teach that the method further comprises FRET labeled probes and a step of monitoring fluorescence from FRET probes, where in the target is no greater than 25 nucleotides (see col. 68, line 10-67).

With regard to claim 39, Wittwer et al. teach that the amplifying and monitoring occur in a closed tube and no reagents are added to the tube subsequent to initiation of amplification (see col. 30, line 30-67, col. 31, line 1-4).

With regard to claims 40-43, Wittwer et al. teach that the monitoring step comprising melting curve analysis occurs during and post amplification step (see col. 40, line 1-65, col. 43, line 22-67, col. 44, line 1-18).

With regard to claim 43, Wittwer et al. teach that the monitoring step comprises determining whether the target has same sequence as a second nucleic acid (see col. 67, line 13-60).

With regard to claim 45-48, Wittwer et al. teach that the method comprises normalizing

melting curve repeating the mixing, amplifying steps with at least one additional target nucleic acid and comparing the normalized melting curves and plotting the fluorescence difference between the normalized curves superimposing a portion of the curve and plotting the fluorescence difference between the curves (see col. 71, line 15-67, col. 17, line 1-46, Fig. 13-26). Accordingly Wittwer et al. anticipates the instant claims.

Claim Rejections - 35 USC § 103

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 29, 49-51, 53, 55-58, 61, 65-66 are rejected under 35 U.S.C. 103(a) as being unpatentable over Wittwer et al. (USPN. 6, 174,670) in view of Haugland et al. (WO 00/66664).

Wittwer et al. teach a method of PCR analysis as discussed above in section 5.

However Wittwer et al. did not teach a ds DNA binding cyanine dyes as claimed in claims

29, 49-51, 53, 55-58, 61,65-66.

Haugland et al. teach ds DNA binding dyes as cyanine dyes and their use in PCR reactions (see page 2, line 16-38, page 3, line 1-22, page 4, line 1-37, page 5, line 1-30, page 6, line 1-33, page 7, line 1-38).

It would have been prima facie obvious to a person of ordinary skill in the art at the time the invention was made to modify the method of monitoring amplification of a target nucleic acid during PCR as taught by Wittwer et al. with a step of including a cyanine DNA binding dyes to as taught by Haugland et al. for the purpose of enhancing the sensitivity of the detection of a target nucleic acid. One skilled in the art would be motivated to combine the method as disclosed by Wittwer et al. with cyanine dyes as taught by Haugland et al. because Haugland et al. explicitly taught the use of cyanine dyes that exhibit a bathchromic spectral shift (a shift to a longer wavelength) and that are particularly useful for excitation in the wavelength ranges between 500nm and 600nm and absorbance maxima between 530nm and 550nm (see page 1, line 25-32) . The ordinary artisan would have had a reasonable expectation of success that inclusion of cyanine dyes would result in enhancing the sensitivity of the detection of a target nucleic acid by shifting to a longer wavelength as suggested by Haugland et al. and such modification of the method would be obvious over the cited prior art.

Conclusion

No claims are allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Suryaprabha Chunduru whose telephone number is 571-272-0783. The examiner can normally be reached on 8.30A.M. - 4.30P.M , Mon - Friday,.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on 571-272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Suryaprabha Chunduru
Primary Examiner
Art Unit 1637

Suryaprabha Chunduru
SURYAPRABHA CHUNDURU 7/23/07
PRIMARY EXAMINER